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A domain constrained deformable (DoCD) model for co-registration of pre- and post-radiated prostate MRI

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ABSTRACT

External beam radiation treatment (EBRT) is a popular method for treating prostate cancer (CaP) involving destroying tumor cells with ionizing radiation. Following EBRT, biochemical failure has been linked with disease recurrence. However, there is a need for methods for evaluating early treatment related changes to allow for an early intervention in case of incomplete disease response. One method for looking at treatment evaluation is to detect changes in MRI markers on a voxel-by-voxel basis following treatment. Changes in MRI markers may be correlated with disease recurrence and complete or partial response. In order to facilitate voxel-by-voxel imaging related treatment changes, and also to evaluate morphologic changes in the gland post treatment, the pre- and post-radiated MRI must first be brought into spatial alignment via image registration. However, EBRT induces changes in the prostate volume and distortion to the internal anatomy of the prostate following radiation treatment. The internal substructures of the prostate, the central gland (CG) and peripheral zone (PZ), may respond to radiation differently, and their resulting shapes may change drastically. Biomechanical models of the prostate that have been previously proposed tend to focus on how external forces affect the surface of the prostate (not the internals), and assume that the prostate is a volume-preserving entity. In this work we present DoCD, a biomechanical model for automatically registering pre-, post-EBRT MRI with the aim of expressly modeling the (1) changes in volume, and (2) changes to the CG and PZ. DoCD was applied to a cohort of 30 patients and achieved a root mean square error of 2.994 mm, which was statistically significantly better a traditional biomechanical model which did not consider changes to the internal anatomy of the prostate (mean of 5.071 mm).

1. Background

Following a diagnosis of prostate cancer (CaP), several treatment options are available [1]. These include brachytherapy, focal ablation therapy, hormonal therapy, external beam radiation therapy (EBRT), and radical prostatectomy [1]. EBRT involves irradiating the affected anatomical region with ionizing radiation, in an effort to destroy CaP cells. During treatment, the radiation disrupts the natural mitotic process in cells [2]. When apoptosis naturally occurs, the tumor cells have not had a chance to divide as rapidly, and therefore get eliminated naturally. Since tumor cells divide at a faster rate than benign cells [3], the radiation implicitly affects tumor cells more than benign cells, and can be effective at reducing the tumor volume. There is also significantly gland shrinkage following the radiation treatment period due to the elimination of tumor cells, as well as atrophy which can also occur to benign prostatic tissue [4].

Yet EBRT may not be effective at completely eradicating CaP, as there may be either residual disease or local recurrence following EBRT [5]. To determine whether EBRT was effective, Prostate Specific Antigen (PSA) concentrations (in ng/ml) are tracked post-EBRT. PSA values are currently used to evaluate treatment efficacy [6], in which a rise in PSA levels post-EBRT is deemed to constitute biochemical failure. Approximately one-fourth of EBRT patients undergo biochemical failure [7].

However, PSA cannot typically be used to evaluate early treatment response. Determining early treatment response in the cases of residual or recurrent disease is necessary to allow for an early image guided intervention which will allow for complete disease response. PSA is usually measured at intervals of 3–6 months [7]. For favorable risk patients, the median PSA doubling time (PSA-DT), a useful

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prognostic tool, is 18 months, and 8 months for unfavorable risk patients [7]. In addition, a PSA-DT of less than 10 months is considered rapid [8]. Consequently there appears to exist a need for a way of assessing very early treatment changes to be able to modulate therapy if necessary via an image guided intervention.

MRI has shown to be useful in the detection of recurrent disease post-EBRT and can potentially be used to discern and quantify treatment efficacy [9–15]. Quantifying voxel-level changes within the tumor region on MRI can potentially be used to quantify early treatment related changes [16]. Foltz et al. [16] studied the association between changes in T2-w and apparent diffusion coefficient (ADC) MRI parameters following EBRT. The tumor was manually identified on pre-EBRT MRI, and mapped onto the post-EBRT MRI The changes in MRI parameter values 6 weeks following treatment were statistically significantly correlated with PSA velocity values (ng/ml/year), suggesting that early changes in voxel-by-voxel MRI imaging markers could be used to predict biochemical treatment response [16].

To determine voxel level changes in imaging markers, one must first register, or spatially align, the pre- and post-EBRT imagery. Registration will allow one to (1) accurately localize the tumor region to study, so as not to confuse changes in tumor appearance with radiation necrosis of benign tissue, (2) determine precise voxel-by-voxel changes in imaging markers, and (3) determine EBRT induced morphologic changes to the prostate. Yet registration of EBRT MRI is not a trivial task, due to changes in MRI intensity values, atrophic shrinkage resulting from radiation, and local morphologic changes occurring within the gland [4] (Fig. 1). While registration was performed manually in [16], manual registration is time-consuming, may be prone to errors and inter-observer variability, and may be infeasible for large-scale studies. This work aims to create a domain constrained deformable (DoCD) biomechanical model to automatically register pre-, post-EBRT MRI in order to study early treatment related changes. The EBRT induced shrinkage effects and changes to the internal structures of the prostate are used create a domain-specific biomechanical model. This model is then used to register pre-, post-EBRT MRI for (1) determining voxel-by-voxel changes, and (2) quantify changes in gland morphology (not just volume) following radiation.

The rest of the paper is organized as follows. In Section 2 we discuss the motivation for our approach. In Section 3 we summarize the closest relate works in which biomechanical models have been used either to model prostate deformations, or model radiation effects on MRI. In Section 4 we describe the DoCD methodology in detail. In Section 5 we describe the data, experiments, and comparative strategies, the results of which are presented in Section 6. In Section 7 we offer concluding remarks and future directions.

2. Motivation and overview of approach

The prostate gland consists of internal structures including the peripheral zone (PZ), central zone (CZ), and transition zone (TZ), where the latter 2 structures are jointly referred to as the central gland (CG) [17]. CG tumors have been found to be significantly less aggressive compared to PZ tumors [18] and the different zones can even have different tissue compositions [19], suggesting that they may respond to EBRT differently. Following EBRT, there can be a significant loss in visible zonal anatomy on MRI [20]. Our DoCD model aims to explicitly exploit domain information by taking into account the different effects EBRT may have on the shapes of the internal prostatic structures, rather than on the gland as a whole.

In [16], outlines of the prostate, tumor, CG, and PZ were manually identified on both the pre- and post-EBRT MRI. Subsequently, the regions so identified were manually brought into alignment between the pre-, post-EBRT MRI. Our DoCD model aims to take advantage of the boundaries of internal structures CG and PZ to develop a domain constrained biomechanical model for automatically registering pre- and post-EBRT MRI. In this work we employ a finite element model (FEM) as the choice of biomechanical model. The FEM is a biomechanical model which uses physical properties such as elasticity and compressibility to deform one or more objects, in our case the CG and PZ.

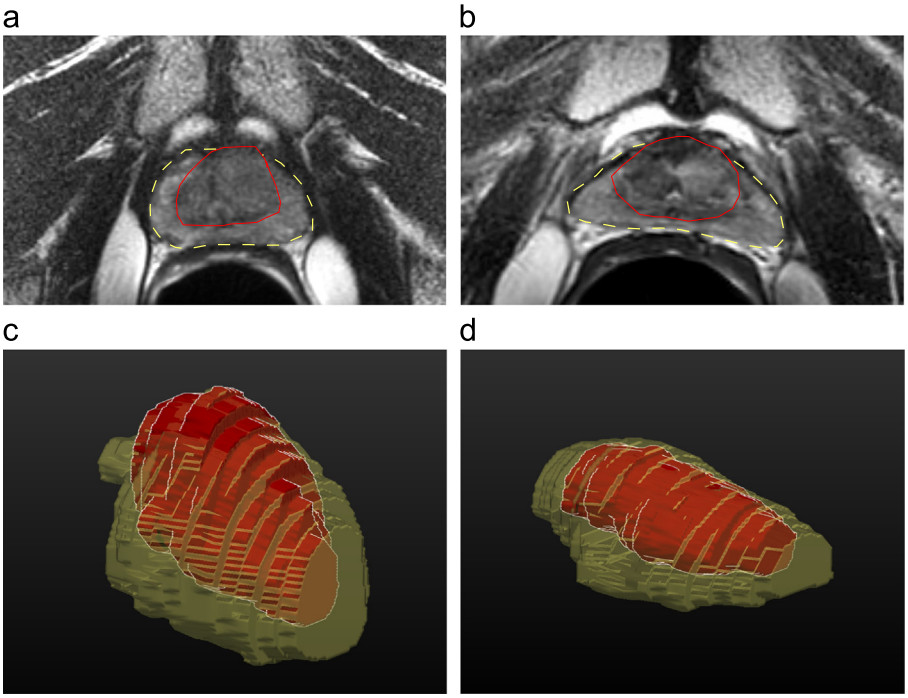

Fig. 1. Prostate MRI intensity changes as a result of EBRT, where the PZ boundary is shown with a dotted yellow outline, and the CG boundary with a solid red outline in (a) and (b). (a) and (c) show the pre-EBRT MRI and (b) and (d) show the post-EBRT MRI. In (c) and (d) 3D renderings of the CG (red) and PZ (yellow) are shown. It can be seen that there are not only significant changes in volume to the prostate as a whole following EBRT, but also changes to the shapes of the PZ and CG, which DoCD aims to model. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)